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VIA ECF & FEDEX

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The Honorable Patty Shwartz, U.S.M.J.
United States District Court
U.S.P.O. & Courthouse Bldg., Room 477
One Federal Square
Newark, New Jersey 07102

Re: *Prometheus Laboratories Inc. v. Roxane Laboratories, Inc.*
Civil Action No. 11-1241 (FSH)(PS)

Dear Judge Shwartz:

This firm, together with Jones Day, represents Plaintiff Prometheus Laboratories Inc. ("Prometheus") in the above-captioned matter. We write in response to defendant Roxane Laboratories, Inc's ("Roxane") opposition to Prometheus' request for leave to amend Its Complaint. (D.I. 43).

Roxane's primary opposition argument asks the Court to consider — on the merits — whether Cipla, Ltd.'s ("Cipla") manufacturing process infringes United States Patent No. 6,175,014 (the "'014 patent"). Specifically, Roxane asks the Court to find the proposed amendments futile notwithstanding documentary evidence produced from its own files showing that Cipla's manufacturing process infringes the '014 patent. As discussed in more detail below, Roxane's arguments are legally and factually flawed. Roxane's jurisdictional arguments and its half-hearted allegations of prejudice and delay also have no merit. Accordingly, Prometheus' request for leave to amend should be granted.

A. The Documents Produced By Roxane Show That Cipla Practices Each Step In The '014 Patent Manufacturing Process

There is no dispute that Prometheus' proposed amendments state a factually and legally valid claim for infringement of the '014 patent. As such, this should be the end of the inquiry. As discussed in Prometheus' request for leave to amend, a proper futility analysis requires

accepting Prometheus' allegations of infringement as true. *See Brown v. Philip Morris Inc.*, 250 F.3d 789, 796 (3d Cir. 2001) (the Court must "accept as true all of the factual allegations in the [proposed amended] complaint as well as the reasonable inferences that can be drawn from them"). The merits of Prometheus' infringement allegations should be litigated after Cipla is joined to this action and the parties have the opportunity to conduct fact and expert discovery regarding its manufacturing process, not in the context of a motion to amend the pleadings.

Nevertheless, Roxane's arguments fail even if the Court were to ignore this well-established standard and look outside the four corners of Prometheus' proposed amended complaint. There is no dispute that the documents concerning Cipla's manufacturing process produced from Roxane's own files show infringement. This bears repeating. The only portion of Cipla's Drug Master File ("DMF") that either party has access to shows infringement. Claim 1 of the '014 patent is directed to a process for manufacturing a class of compounds that includes alosetron hydrochloride, the active ingredient in Roxane's ANDA product. [redacted] The process of Claim 1 is a reaction between what the patent refers to as compounds of formula (II) and formula (III). [redacted] Accordingly, Cipla's manufacturing process infringes at least Claim 1 of the '014 patent.

Remarkably, Roxane does not deny that its ANDA documents show infringement of the '014 patent. (D.I. 43 at 6-8.) Instead, it asks Prometheus and this Court to accept unsupported representations that Cipla is allegedly doing something different from what is described in the document that was provided to the FDA. Roxane's unsupported argument is not evidence, and should not foreclose Prometheus' opportunity to litigate its claims of infringement concerning the '014 patent. This is especially true in a case such as this one where the existing documentary evidence clearly and indisputably shows infringement.

B. This Court Has Subject Matter Jurisdiction Over Prometheus' Amended Claims

Roxane contends that this Court does not have subject matter jurisdiction over Prometheus' proposed amended claims under 35 U.S.C. § 271(e)(2)(A) or under the Declaratory Judgment Act. (D.E. 43 at 8-11.) These arguments have no merit. As discussed below, the Court of Appeals for the Federal Circuit has upheld similar claims for infringement under Section 271(e)(2) and under the Declaratory Judgment Act. Accordingly, Roxane's jurisdictional futility arguments should also be rejected.

1. Section 271(e)(2) Supports A Claim Against Cipla And Byron For Contributory Infringement

Prometheus' proposed amendments include allegations that Cipla and Byron Chemical Co., Inc. ("Byron") contributorily infringe U.S. Patent No. 7,284,770 (the "'770 patent"). (*See* D.I. 38 at Ex. A (Prometheus' First Amended Complaint at ¶ 44)). The '770 patent is the same patent already in suit in this action and that is currently being enforced against Roxane. It is directed to methods of using the drug alosetron hydrochloride for the treatment of Irritable Bowel Syndrome ("IBS"). As discussed above, [redacted] Consequently, Cipla and Byron are contributing to Roxane's filing of its ANDA, which is an act of infringement under § 271(e)(2).

Without citing any authority, Roxane argues that a claim for contributory infringement cannot be made against Cipla and Byron under § 271(e)(2) because they have not filed an ANDA with a Paragraph IV certification. (D.I. 43 at 11.) This very argument has already been rejected by the Court of Appeals for the Federal Circuit. Indeed, the Court did so in a case involving Cipla. *See Forest Labs. v. Ivax Pharmaceuticals, Inc.*, 501 F.3d 1263, 1272 (Fed. Cir. 2007) (finding that "Cipla is as culpable, and hence entitled to be enjoined, as [the ANDA filer]"). The Federal Circuit specifically held that § 271(e)(2) may support an action for patent infringement against the supplier of API that contributes to the infringement by the ANDA filer:

> Cipla is providing information, and will provide material, that [the ANDA filer] will use to obtain FDA approval. . . . They are partners. Cipla would be contributing to the infringement by [the ANDA filer], so the injunction should cover both partners.

Id. The Southern District of New York reached a similar conclusion earlier this year in connection with granting a motion to join Cipla to an ANDA litigation. *Gilead Sciences, Inc. v. Teva Pharmaceuticals USA Inc.*, 2011 WL 2462764, at *2-3 (S.D.N.Y. June 13, 2011) (rejecting futility arguments based on the safe harbor provision of the Hatch-Waxman Act). Accordingly, this Court has subject matter jurisdiction over Prometheus' amended allegations of infringement against Cipla and Byron concerning the '770 patent.

2. Cipla and Byron Are Offering Alosetron For Sale In The United States

Contrary to Roxane's contention, this Court also has jurisdiction over Prometheus' proposed amendments concerning infringement of the '014 patent under 35 U.S.C. § 271(g). (*See* D.I. 43 at 9.) Prometheus' proposed amendments include allegations that Byron and Cipla

are importing product made by an infringing method into the United States. This is supported by Byron's website that "invite[s] [the customer] to make use of [its] API (active pharmaceutical ingredient) data base below," which includes alosetron. (*See* Ex. B, Byron Chemical Products & Search API at http://www.byronchem.com/human.php (last visited Oct. 12, 2011.) This is precisely the type of conduct prohibited by § 271(g). Roxane contends that "there has been no infringing activity under Section 271(g)," yet it has offered no proof that this is the case. Indeed it is difficult to understand how Roxane's counsel could make such a representation given that it does not represent Cipla or Byron. (*See* D.I. 43 at 9.) In any event, Prometheus should be allowed to discover the full scope of Byron's and Cipla's activities once they are joined to this action.

3. This Court Has Declaratory Judgment Jurisdiction Over Defendants' Infringement Of "Method of Making" Patents Like The '014 Patent

Roxane also argues that there is no "case or controversy" concerning the defendants' alleged infringement of the '014 patent to support this Court's jurisdiction under the Declaratory Judgment Act. (D.I. 43 at 8). These arguments are legally baseless. Indeed, in *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1571 (Fed. Cir. 1997) the Court of Appeals for the Federal Circuit rejected the very same arguments under factual circumstances that are remarkably similar to those presented here.

Like this case, *Novopharm* was an ANDA case in which the patentee sought a declaration that the importation of API manufactured according to a patented process, after FDA approval, would violate 35 U.S.C. § 271(g). *Id.* at 1570. The Federal Circuit rejected the defendant's arguments that the district court did not have jurisdiction under the Declaratory Judgment Act to adjudicate these types of claims. The Court explained that:

> Some of Novopharm's acts that form the basis of the declaratory judgment action are of course protected from liability for infringement under § 271(e)(1)[]. Nevertheless, the protected status of Novopharms activities leading to its submissions to the FDA does not by itself prevent the district court from considering Glaxos' request for declaratory relief because such relief is directed to the time after the ANDA is approved, when § 271(e)(1) no longer provides a shelter against infringement liability. Accordingly, declaratory relief is available to the patentee asserting a "method of making" claim if, as here, sufficient facts are alleged to create an actual case or controversy.

Id. at 1571. The Court also found that the generic manufacturers' systematic attempts "to meet the applicable regulatory requirements while preparing to import its product," supported the conclusion that the patentee's injury was sufficiently imminent to support jurisdiction. *Id.*

This Court has jurisdiction over the amended allegations of infringement of the '014 patent for similar reasons. The '014 patent is directed to "methods of making" alosetron hydrochloride that will be used in Roxane's proposed ANDA product. As in *Novopharm*, [redacted] Accordingly, a "case or controversy" exists between Prometheus and the defendants concerning infringement of the '014 patent that will take place after the approval of Roxane's ANDA products.

The cases relied upon by Roxane are not to the contrary. For example, the *Eisai* case expressly distinguishes itself from *Novopharm* and other cases like this one involving "methods of making" patents. *See Eisai Co. v. Mutual Pharm. Co.*, No. 06-3613, 2007 WL 4556958, at *19 (D.N.J. Dec. 20, 2007) ("*Novopharm* concerned a 'method of making' patent claim, which is not covered by § 271(e)(2) . . . . Here, § 271(e)(2) applies . . . ."). Meanwhile, the *Sierra Applied Sciences, Inc. v. Advanced Energy Indus., Inc.* and *In re Rosuvastatin Calcium Patent Litig.* cases fail to even address declaratory judgment jurisdiction over claims that generic manufacturers infringe "method of making" patents. 363 F.3d 1361, 1379-80 (Fed. Cir. 2004); No. 08-1949, 2008 WL 5046424, at *12-13 (D. Del. Nov. 24, 2008). As discussed above, this is the province of *Novopharm*. *See* 110 F.3d at 1571 ("[D]eclaratory relief is available to the patentee asserting a 'method of making' claim if . . . sufficient facts are alleged to create an actual case or controversy."). Accordingly, this Court has jurisdiction over Prometheus' allegations of infringement concerning the '014 patent under the Declaratory Judgment Act.

C. There Is No Undue Prejudice

The Third Circuit has stressed that "[p]rejudice . . . means undue difficulty in prosecuting a lawsuit as a result of a change of tactics or theories on the part of the other party." *Deakyne v. Commissioners of Lewes*, 416 F.2d 290, 300 (3d. Cir. 1969). Roxane's opposition fails to identify how the amendments would make it unduly difficult for Roxane to defend itself. Its allegations that the proposed amendments will require additional discovery and expense are true of virtually every amendment and do not support a claim of prejudice. Moreover, this case is still in the early stages of discovery. Document production is ongoing, not a single deposition has taken place and a trial is likely more than a year away. Accordingly, there is no undue prejudice that should weigh in favor of denying Prometheus' request.

D. There Has Been No Undue Delay

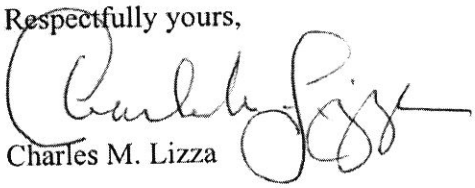
Finally, Prometheus' proposed Amended Complaint will cause no undue delay. Third Circuit law unequivocally provides that "[t]he passage of time, without more, does not require that a motion to amend a complaint be denied . . . ." *Adams v. Gould, Inc.*, 739 F.2d 858, 868 (3d Cir. 1984). At its core, Roxane's argument is nothing more than an attempt to use mere "passage of time" to deny Prometheus' proposed Amended Complaint. Roxane admits that the discovery relevant to Prometheus' instant Motion was not produced until May 2011. (D.I. 43 at

12.) Without referencing any authority from this District or otherwise, Roxane argues that Prometheus filing its motion approximately four months after it uncovered the relevant discovery is somehow an "undue delay." There was no delay. During that four month period, Prometheus requested discovery from Roxane concerning Cipla's manufacturing process and worked to develop additional evidence supporting its amended claims. After Roxane refused to provide the requested discovery, Prometheus requested leave to amend its Complaint in accordance with the time period set out in the Court's Scheduling Order. Accordingly, there is no undue delay that should weigh in favor of denying Prometheus' request.

E. Conclusion

For the foregoing reasons, Prometheus respectfully requests that the Court grant it leave to file an Amended Complaint.

Respectfully yours,



Charles M. Lizza

Exhibits

cc: All counsel (via e-mail)

EXHIBIT A

Confidential Material Redacted
Pursuant to L. Civ. R. 5.3(c)(3)
Motion to Seal Pending

EXHIBIT B

- Home
- Our Company
  - Business Team
  - Message from our President
- Services
  - Regulatory & Drug Import/Distribution
  - Contract Manufacturing & Dosage Formulations
  - Business Development & Network
- Products & Search
  - API "Active Pharmaceutical Ingredients"
  - Human
  - Veterinary
- Contact

Product Name

Type a product name or part of a name

Search

Applications

Include also these applications:

- ☐ Inhalation
- ☐ Injectable
- ☐ Nasal
- ☐ Opthalmic
- ☐ Oral Liquid
- ☐ Oral Solid
- ☐ Topical
- ☐ Other

Categories

Include also these categories:

- ☐ Allergy / Cough-Cold / OTC products
- ☐ Analgesic / Anti-Inflammatory
- ☐ Anti-Infectives
- ☐ Anticonvulsants / Sedatives / Hypnotic Agents
- ☐ Cardiovascular Agents
- ☐ Central Nervous System Agents
- ☐ Cholesterol Agents
- ☐ Dermatologic Products
- ☐ Diabetes Agents
- ☐ Gastrointestinal Agents
- ☐ Oncolytic / Anti-Neoplastic Agents
- ☐ Ophthalmic Agents
- ☐ Osteolytic Agents
- ☐ Psychotherapeutic Agents
- ☐ Respiratory Agents
- ☐ Steroidal / Hormonal Agents

Human (Active Pharmaceutical Ingredients)

Developing Products for Your Market

Byron Chemical offers you the mix of expertise throughout the entire life cycle of your product or project. From API development and regulatory functions to commercialization with ongoing market intelligence, our staff and business team provide individualized functions to support your projects. Our sourcing and supply services ensure that you are provided with the optimal products.

Our Human APIs are sourced from international manufactures that are specifically selected by our experts for chemistry type, regulatory compliance, and timeline management. Various chemistries and capabilities noted within our list below includes: Steroids (including sterile), Prostaglandins, Polypeptides, Containment type drugs, Hormonal, Fermentation, and Controlled Drugs.

The facilities selected are screened for compliance to strict regulatory and quality standards – most of which adhere to US and EU regulatory authorities.

Our sourcing approach considers essential time management during the entire development. Whether your project requires a fast track approach to the generic market or

☐ Other

Search

perhaps a second source supply position, Byron Chemical Company is pleased to service your needs. We invite you to make use of our API (active pharmaceutical ingredient) data base below, which includes items in commercial and development production stages.

**Products under patent are available for such R&D use in the USA as permitted under Section 35 USC ¶ 271 (e) (1).*

Available Products

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

	Product	Category	Applications
☐	16a-Bromoepiandrosterone	Other	Other
☐	4-Aminopyridine	Other	Other
☐	4-Phenylbutyric Acid	Cholesterol Agents	Other
☐	Abacavir	Anti-Infectives	Oral Solid, Oral Liquid
☐	Acamprosate Calcium	Other	Oral Solid
☐	Acetaminophen	Analgesic / Anti-Inflammatory	Oral Solid, Oral Liquid, Other
☐	Acetylsalicylic Acid Lysine Salt	Analgesic / Anti-Inflammatory	Oral Solid
☐	Acyclovir Sodium	Anti-Infectives, Dermatologic Products	Oral Liquid, Topical, Injectable, Oral Solid
☐	Adapalene	Anti-Infectives, Dermatologic Products	Topical
☐	Adefovir Dipivoxil	Anti-Infectives	Oral Solid
☐	Alarelin	Steroidal / Hormonal Agents	Injectable
☐	Albendazol	Anti-Infectives	Oral Solid
☐	Albuterol	Respiratory Agents	Inhalation, Oral Solid, Oral Liquid
☐	Albuterol Sulfate	Respiratory Agents	Oral Solid, Oral Liquid, Inhalation
☐	Alclometasone Dipropionate	Analgesic / Anti-Inflammatory, Steroidal / Hormonal Agents, Dermatologic Products	Topical
☐	Aldosterone	Steroidal / Hormonal Agents	Other
☐	Alendronate Sodium	Osteolytic Agents	Oral Solid, Oral Liquid
☐	Alfuzocin HCl	Cardiovascular Agents	Oral Solid
☐	Aliskiren Hemifumarate	Cardiovascular Agents	Oral Solid
☐	Allopurinol	Other	Oral Solid, Injectable
☑	Alosetron	Gastrointestinal Agents	Oral Solid
☐	Alprazolam	Anti-Anxiety, Central Nervous System Agents	Oral Liquid, Oral Solid
☐	Alprostadil	Other	Injectable, Other
☐	Amantadine HCl	Anti-Infectives	Oral Liquid, Oral Solid
☐	Amcinonide	Analgesic / Anti-Inflammatory, Steroidal / Hormonal Agents, Dermatologic Products	Topical
☐	Amifostine	Oncolytic / Anti-Neoplastic Agents	Injectable
☐	Amlodipine Besylate	Cardiovascular Agents	Oral Solid
☐	Amlodipine Mesylate	Cardiovascular Agents	Oral Solid
☐	Amoxapine	Anti-Depressants, Central Nervous System Agents	Oral Solid
☐	Anagrelide HCl	Other	Oral Solid